

## WEST Search History

DATE: Tuesday, March 01, 2005

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L7	L1 and theophylline	12
<input type="checkbox"/>	L6	Group I and theophylline	229
<input type="checkbox"/>	L5	Group I and aptamer	245
<input type="checkbox"/>	L4	L1 and L2 and L3	78
<input type="checkbox"/>	L3	effector	34955
<input type="checkbox"/>	L2	aptamer	3615
<input type="checkbox"/>	L1	Group I intron	818

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 10:34:39 ON 01 MAR 2005)

FILE 'MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 10:36:08 ON 01 MAR  
2005

L1        2528 S GROUP I INTRON  
L2        3305 S APTAMER  
L3        152309 S EFFECTOR  
L4        1 S L1 AND L2 AND L3  
L5        10 S L1 AND L2  
L6        6 DUP REM L5 (4 DUPLICATES REMOVED)  
L7        14 GROUP I AND APTAMER  
L8        10 DUP REM L7 (4 DUPLICATES REMOVED)  
L9        3 L1 AND THEOPHY?  
L10      3 DUP REM L9 (0 DUPLICATES REMOVED)  
L11      65 T4 INTRON  
L12      0 L11 AND THEOPHY?  
L13      187 TD INTRON  
L14      0 L13 AND THEOPHY  
L15      0 L11 AND APTAMER  
L16      0 L13 AND APTAMER

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:22547 CAPLUS  
DOCUMENT NUMBER: 138:282224  
TITLE: Group I aptazymes as genetic regulatory switches  
AUTHOR(S): Thompson, Kristin M.; Syrett, Heather A.; Knudsen, Scott M.; Ellington, Andrew D.  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX, 78712, USA  
SOURCE: BMC Biotechnology [online computer file] (2002), 2, No pp. given  
CODEN: BBMIE6; ISSN: 1472-6750  
URL: <http://www.biomedcentral.com/1472-6750/2/21>  
PUBLISHER: BioMed Central Ltd.  
DOCUMENT TYPE: Journal; (online computer file)  
LANGUAGE: English  
AB Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated in vitro by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication in vivo. We attempted to generate Group I self-splicing introns that were activated by a small organic effector, theophylline, and to show that such Group I aptazymes could mediate theophylline-dependent splicing in vivo. By appending aptamers to the Group I self-splicing intron, we have generated a Group I aptazyme whose in vivo splicing is controlled by exogenously added small mols. Substantial differences in gene regulation could be observed with compds. that differed by as little as a single Me group. The effector -specificity of the Group I aptazyme could be rationally engineered for new effector mols. In conclusion, group I aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies.  
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 10:34:39 ON 01 MAR 2005)

FILE 'MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 10:36:08 ON 01 MAR 2005

L1 2528 S GROUP I INTRON  
L2 3305 S APTAMER  
L3 152309 S EFFECTOR  
L4 1 S L1 AND L2 AND L3

=> s L1 and L2  
L5 10 L1 AND L2

=> dup rem L5  
PROCESSING COMPLETED FOR L5  
L6 6 DUP REM L5 (4 DUPLICATES REMOVED)  
ANSWERS '1-2' FROM FILE MEDLINE  
ANSWERS '3-6' FROM FILE CAPLUS

=> d ibib, abs L6 1-6

L6 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2002004326 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11752347  
TITLE: NCIR: a database of non-canonical interactions in known RNA structures.  
AUTHOR: Nagaswamy Uma; Larios-Sanz Maia; Hury James; Collins

CORPORATE SOURCE: Shakaala; Zhang Zhengdong; Zhao Qin; Fox George E  
Department of Biology and Biochemistry, University of  
Houston, 369 Science and Research Building 2, Houston, TX  
77204-5001, USA.

SOURCE: Nucleic acids research, (2002 Jan 1) 30 (1) 395-7.  
Journal code: 0411011. ISSN: 1362-4962.

PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200201

ENTRY DATE: Entered STN: 20020102  
Last Updated on STN: 20020125  
Entered Medline: 20020121

AB The secondary and tertiary structure of an RNA molecule typically includes a number of non-canonical base-base interactions. The known occurrences of these interactions are tabulated in the NCIR database, which can be accessed from [http://prion.bchs.uh.edu/bp\\_type/](http://prion.bchs.uh.edu/bp_type/). The number of examples is now over 1400, which is an increase of >700% since the database was first published. This dramatic increase reflects the addition of data from the recently published crystal structures of the 50S (2.4 Å) and 30S (3.0 Å) ribosomal subunits. In addition, non-canonical interactions observed in published crystal and NMR structures of tRNAs, **group I introns**, ribozymes, RNA **aptamers** and synthetic oligonucleotides are included. Properties associated with these interactions, such as sequence context, sugar pucker conformation, glycosidic angle conformation, melting temperature, chemical shift and free energy, are also reported when available. Out of the 29 anticipated pairs with at least two hydrogen bonds, 28 have been observed to date. In addition, several novel examples, not generally predicted, have also been encountered, bringing the total of such pairs to 36. Added to this list are a variety of single, bifurcated, triple and quadruple interactions. The most common non-canonical pairs are the sheared GA, GA imino, AU reverse Hoogsteen, and the GU and AC wobble pairs. The most frequent triple interaction connects N3 of an A with the amino of a G that is also involved in a standard Watson-Crick pair.

L6 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 1998097413 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9436913

TITLE: In vitro selection and characterization of streptomycin-binding RNAs: recognition discrimination between antibiotics.

AUTHOR: Wallace S T; Schroeder R

CORPORATE SOURCE: Institute of Microbiology and Genetics, University of Vienna, Austria.

SOURCE: RNA (New York, N.Y.), (1998 Jan) 4 (1) 112-23.  
Journal code: 9509184. ISSN: 1355-8382.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199802

ENTRY DATE: Entered STN: 19980224  
Last Updated on STN: 19980224  
Entered Medline: 19980206

AB As pathogens continue to evade therapeutical drugs, a better understanding of the mode of action of antibiotics continues to have high importance. A growing body of evidence points to RNA as a crucial target for antibacterial and antiviral drugs. For example, the aminocyclitol antibiotic streptomycin interacts with the 16S ribosomal RNA and, in addition, inhibits **group I intron** splicing.

To understand the mode of binding of streptomycin to RNA, we isolated small, streptomycin-binding RNA **aptamers** via in vitro selection.

In addition, bluensomycin, a streptomycin analogue that does not inhibit splicing, was used in a counter-selection to obtain RNAs that bind streptomycin with high affinity and specificity. Although an RNA from the normal selection (motif 2) bound both antibiotics, an RNA from the

counter-selection (motif 1) discriminated between streptomycin and bluensomycin by four orders of magnitude. The binding site of streptomycin on the RNAs was determined via chemical probing with dimethylsulfate and kethoxal. The minimal size required for drug binding was a 46- and a 41-mer RNA for motifs 1 and 2, respectively. Using Pb<sup>2+</sup> cleavage in the presence and absence of streptomycin, a conformational change spanning the entire mapped sequence length of motif 1 was observed only when both streptomycin and Mg<sup>2+</sup> were present. Both RNAs require Mg<sup>2+</sup> for binding streptomycin.

L6 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:473146 CAPLUS  
 DOCUMENT NUMBER: 139:47171  
 TITLE: The modulation of NOGO and NOGO receptor gene expression using antisense and enzymic nucleic acid-based technologies and therapeutic uses  
 INVENTOR(S): Blatt, Lawrence; McSwiggen, James; Chowrira, Bharat  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 780,533.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 14  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003113891	A1	20030619	US 2001-827395	20010405
US 2003060611	A1	20030327	US 2001-780533	20010209
WO 2002081628	A2	20021017	WO 2002-US10512	20020403
WO 2002081628	A3	20030220		
WO 2002081628	C1	20030828		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002081628	A2	20021017	WO 2002-XA10512	20020403
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WO 2002081628	A2	20021017	WO 2002-XB10512	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002081628	A2	20021017	WO 2002-XC10512	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1386004 A2 20040204 EP 2002-763926 20020403  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2003203870 A1 20031030 US 2003-430882 20030506

PRIORITY APPLN. INFO.: US 2000-181797P P 20000211  
US 2001-780533 A2 20010209  
WO 2001-US4273 A2 20010209  
US 2001-827395 A 20010405  
US 2001-294412P P 20010529  
US 2001-315315P P 20010828  
WO 2002-US10512 W 20020403

AB The invention features novel nucleic acid-based mols., including enzymic nucleic acid mols. (ribozymes), antisense nucleic acids, 2'-5A antisense chimeras, triplex DNA, decoy RNA, **aptamers**, antisense nucleic acids containing RNA cleaving chemical groups, and methods to modulate gene expression, for example, genes encoding certain myelin proteins that inhibit or are involved in the inhibition of neurite growth, including axonal regeneration in the CNS. In particular, the instant invention features nucleic-acid based techniques to modulate the expression of NOGO and NOGO receptor genes. Specifically, the invention features the use of nucleic acid-based techniques to specifically inhibit the expression of NOGO gene (Genbank Accession Number AB020693) and NOGO-66 receptor (Genbank Accession Number AF283463). Thus, nucleic acids encoding these products are scanned to identify targets for cleavage by designed enzymic nucleic acids, such as hammerhead ribozymes, Zinzymes, DNAzymes, and Amberzymes. Chemical modifications in the sugar, base, and/or phosphate backbones of these enzymic nucleic acids is carried out to improve their stability.

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:232387 CAPLUS  
DOCUMENT NUMBER: 138:265004  
TITLE: RNA in drug development  
AUTHOR(S): Kozu, Tomoko  
CORPORATE SOURCE: Saitama Cancer Cent. Res. Inst., Japan  
SOURCE: Tanpakushitsu Kakusan Koso (2003), 48(4,  
3Gatsugozaka), 540-548  
CODEN: TAKKAJ; ISSN: 0039-9450  
PUBLISHER: Kyoritsu Shuppan  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review on the principle and clin. application of RNA-based drugs and biosensors, discussing: (1) gene knockdown by using antisense oligonucleotides, ribozymes, dsRNA, siRNA, and group II intron, (2) RNA repair by trans-splicing using **group I intron** and spliceosome, (3) functional modification of proteins (VEGF, coagulation factor IXa, etc.) by RNA **aptamers**, and (4) RNA-based biosensors using allosteric ribozymes, aptazymes, and **aptamers**.

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:22547 CAPLUS  
DOCUMENT NUMBER: 138:282224  
TITLE: Group I aptazymes as genetic regulatory switches  
AUTHOR(S): Thompson, Kristin M.; Syrett, Heather A.; Knudsen, Scott M.; Ellington, Andrew D.  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX, 78712, USA  
SOURCE: BMC Biotechnology [online computer file] (2002), 2, No pp. given  
CODEN: BBMIE6; ISSN: 1472-6750  
URL: <http://www.biomedcentral.com/1472-6750/2/21>  
PUBLISHER: BioMed Central Ltd.  
DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English  
AB Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated *in vitro* by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication *in vivo*. We attempted to generate Group I self-splicing introns that were activated by a small organic effector, theophylline, and to show that such Group I aptazymes could mediate theophylline-dependent splicing *in vivo*. By appending **aptamers** to the Group I self-splicing intron, we have generated a Group I aptazyme whose *in vivo* splicing is controlled by exogenously added small mols. Substantial differences in gene regulation could be observed with compds. that differed by as little as a single Me group. The effector-specificity of the Group I aptazyme could be rationally engineered for new effector mols. In conclusion, group I aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:490324 CAPLUS

TITLE: New insights into RNA folding from structures of small RNAs

AUTHOR(S): Feigon, J.

CORPORATE SOURCE: Department Chemistry & Biochemistry, University California, Los Angeles, CA, 90095-1569, USA

SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), PHYS-162. American Chemical Society: Washington, D. C.

CODEN: 64RNAO

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Recent solution NMR structures of RNA oligonucleotides provide a wealth of information in the factors underlying RNA folding and stability. We have used multinuclear, multidimensional NMR to solve the structure of several RNAs, including an ATP-binding RNA **aptamer**, a rRNA stem-loop, and the tetraloop receptor of a **Group I intron**.

The structures, and what they tell us about RNA folding, will be discussed.

=> d his

(FILE 'HOME' ENTERED AT 10:34:39 ON 01 MAR 2005)

FILE 'MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 10:36:08 ON 01 MAR 2005

L1 2528 S GROUP I INTRON

L2 3305 S APTAMER

L3 152309 S EFFECTOR

L4 1 S L1 AND L2 AND L3

L5 10 S L1 AND L2

L6 6 DUP REM L5 (4 DUPLICATES REMOVED)

=> group I and aptamer

L7 14 GROUP I AND APTAMER

=> dup rem L7

PROCESSING COMPLETED FOR L7

L8 10 DUP REM L7 (4 DUPLICATES REMOVED)

ANSWERS '1-3' FROM FILE MEDLINE

ANSWERS '4-9' FROM FILE CAPLUS

ANSWER '10' FROM FILE EMBASE

=> d ibib, abs L8 1-10

L8 ANSWER 1 OF 10 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2002004326 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11752347  
TITLE: NCIR: a database of non-canonical interactions in known RNA structures.  
AUTHOR: Nagaswamy Uma; Larios-Sanz Maia; Hury James; Collins Shakaala; Zhang Zhengdong; Zhao Qin; Fox George E  
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Houston, 369 Science and Research Building 2, Houston, TX 77204-5001, USA.  
SOURCE: Nucleic acids research, (2002 Jan 1) 30 (1) 395-7.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200201  
ENTRY DATE: Entered STN: 20020102  
Last Updated on STN: 20020125  
Entered Medline: 20020121

AB The secondary and tertiary structure of an RNA molecule typically includes a number of non-canonical base-base interactions. The known occurrences of these interactions are tabulated in the NCIR database, which can be accessed from [http://prion.bchs.uh.edu/bp\\_type/](http://prion.bchs.uh.edu/bp_type/). The number of examples is now over 1400, which is an increase of >700% since the database was first published. This dramatic increase reflects the addition of data from the recently published crystal structures of the 50S (2.4 Å) and 30S (3.0 Å) ribosomal subunits. In addition, non-canonical interactions observed in published crystal and NMR structures of tRNAs, group I introns, ribozymes, RNA aptamers and synthetic oligonucleotides are included. Properties associated with these interactions, such as sequence context, sugar pucker conformation, glycosidic angle conformation, melting temperature, chemical shift and free energy, are also reported when available. Out of the 29 anticipated pairs with at least two hydrogen bonds, 28 have been observed to date. In addition, several novel examples, not generally predicted, have also been encountered, bringing the total of such pairs to 36. Added to this list are a variety of single, bifurcated, triple and quadruple interactions. The most common non-canonical pairs are the sheared GA, GA imino, AU reverse Hoogsteen, and the GU and AC wobble pairs. The most frequent triple interaction connects N3 of an A with the amino of a G that is also involved in a standard Watson-Crick pair.

L8 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 1998097413 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9436913  
TITLE: In vitro selection and characterization of streptomycin-binding RNAs: recognition discrimination between antibiotics.  
AUTHOR: Wallace S T; Schroeder R  
CORPORATE SOURCE: Institute of Microbiology and Genetics, University of Vienna, Austria.  
SOURCE: RNA (New York, N.Y.), (1998 Jan) 4 (1) 112-23.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199802  
ENTRY DATE: Entered STN: 19980224  
Last Updated on STN: 19980224  
Entered Medline: 19980206

AB As pathogens continue to evade therapeutical drugs, a better understanding of the mode of action of antibiotics continues to have high importance. A growing body of evidence points to RNA as a crucial target for antibacterial and antiviral drugs. For example, the aminocyclitol antibiotic streptomycin interacts with the 16S ribosomal RNA and, in

addition, inhibits **group I** intron splicing. To understand the mode of binding of streptomycin to RNA, we isolated small, streptomycin-binding RNA **aptamers** via *in vitro* selection. In addition, bluensomycin, a streptomycin analogue that does not inhibit splicing, was used in a counter-selection to obtain RNAs that bind streptomycin with high affinity and specificity. Although an RNA from the normal selection (motif 2) bound both antibiotics, an RNA from the counter-selection (motif 1) discriminated between streptomycin and bluensomycin by four orders of magnitude. The binding site of streptomycin on the RNAs was determined via chemical probing with dimethylsulfate and kethoxal. The minimal size required for drug binding was a 46- and a 41-mer RNA for motifs 1 and 2, respectively. Using Pb<sup>2+</sup> cleavage in the presence and absence of streptomycin, a conformational change spanning the entire mapped sequence length of motif 1 was observed only when both streptomycin and Mg<sup>2+</sup> were present. Both RNAs require Mg<sup>2+</sup> for binding streptomycin.

L8 ANSWER 3 OF 10 MEDLINE on STN  
ACCESSION NUMBER: 2003506056 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12466025  
TITLE: **Group I** aptazymes as genetic regulatory switches.  
AUTHOR: Thompson Kristin M; Syrett Heather A; Knudsen Scott M; Ellington Andrew D  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX 78712, USA.. kthompson@archemix.com  
CONTRACT NUMBER: 1R01 GM61789-01 (NIGMS)  
SOURCE: BMC biotechnology [electronic resource], (2002 Dec 4) 2 (1) 21. Electronic Publication: 2002-12-04.  
Journal code: 101088663. ISSN: 1472-6750.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200312  
ENTRY DATE: Entered STN: 20031030  
Last Updated on STN: 20031219  
Entered Medline: 20031208  
AB BACKGROUND: Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated *in vitro* by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication *in vivo*. We attempted to generate **Group I** self-splicing introns that were activated by a small organic effector, theophylline, and to show that such **Group I** aptazymes could mediate theophylline-dependent splicing *in vivo*.  
RESULTS: By appending **aptamers** to the **Group I** self-splicing intron, we have generated a **Group I** aptazyme whose *in vivo* splicing is controlled by exogenously added small molecules. Substantial differences in gene regulation could be observed with compounds that differed by as little as a single methyl group. The effector-specificity of the **Group I** aptazyme could be rationally engineered for new effector molecules. CONCLUSION: **Group I** aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies.

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:473146 CAPLUS  
DOCUMENT NUMBER: 139:47171  
TITLE: The modulation of NOGO and NOGO receptor gene expression using antisense and enzymic nucleic acid-based technologies and therapeutic uses  
INVENTOR(S): Blatt, Lawrence; McSwiggen, James; Chowrira, Bharat  
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S.  
 Ser. No. 780,533.  
 CODEN: USXXCO

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 14  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003113891	A1	20030619	US 2001-827395	20010405
US 2003060611	A1	20030327	US 2001-780533	20010209
WO 2002081628	A2	20021017	WO 2002-US10512	20020403
WO 2002081628	A3	20030220		
WO 2002081628	C1	20030828		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002081628	A2	20021017	WO 2002-XA10512	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002081628	A2	20021017	WO 2002-XB10512	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002081628	A2	20021017	WO 2002-XC10512	20020403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1386004	A2	20040204	EP 2002-763926	20020403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003203870	A1	20031030	US 2003-430882	20030506
PRIORITY APPLN. INFO.:			US 2000-181797P	P 20000211
			US 2001-780533	A2 20010209
			WO 2001-US4273	A2 20010209
			US 2001-827395	A 20010405
			US 2001-294412P	P 20010529
			US 2001-315315P	P 20010828
			WO 2002-US10512	W 20020403

AB The invention features novel nucleic acid-based mols., including enzymic nucleic acid mols. (ribozymes), antisense nucleic acids, 2-5A antisense

chimeras, triplex DNA, decoy RNA, **aptamers**, antisense nucleic acids containing RNA cleaving chemical groups, and methods to modulate gene expression, for example, genes encoding certain myelin proteins that inhibit or are involved in the inhibition of neurite growth, including axonal regeneration in the CNS. In particular, the instant invention features nucleic-acid based techniques to modulate the expression of NOGO and NOGO receptor genes. Specifically, the invention features the use of nucleic acid-based techniques to specifically inhibit the expression of NOGO gene (Genbank Accession Number AB020693) and NOGO-66 receptor (Genbank Accession Number AF283463). Thus, nucleic acids encoding these products are scanned to identify targets for cleavage by designed enzymic nucleic acids, such as hammerhead ribozymes, Zinzymes, DNAzymes, and Amberzymes. Chemical modifications in the sugar, base, and/or phosphate backbones of these enzymic nucleic acids is carried out to improve their stability.

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:232387 CAPLUS  
DOCUMENT NUMBER: 138:265004  
TITLE: RNA in drug development  
AUTHOR(S): Kozu, Tomoko  
CORPORATE SOURCE: Saitama Cancer Cent. Res. Inst., Japan  
SOURCE: Tanpakushitsu Kakusan Koso (2003), 48(4,  
3Gatsugozaka), 540-548  
CODEN: TAKKAJ; ISSN: 0039-9450  
PUBLISHER: Kyoritsu Shuppan  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review on the principle and clin. application of RNA-based drugs and biosensors, discussing: (1) gene knockdown by using antisense oligonucleotides, ribozymes, dsRNA, siRNA, and group II intron, (2) RNA repair by trans-splicing using **group I** intron and spliceosome, (3) functional modification of proteins (VEGF, coagulation factor IXa, etc.) by RNA **aptamers**, and (4) RNA-based biosensors using allosteric ribozymes, aptazymes, and **aptamers**.

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:840940 CAPLUS  
DOCUMENT NUMBER: 139:18938  
TITLE: A versatile communication module for controlling RNA folding and catalysis  
AUTHOR(S): Kertsburg, Alexis; Soukup, Garrett A.  
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University, Omaha, NE, 68178, USA  
SOURCE: Nucleic Acids Research (2002), 30(21), 4599-4606  
CODEN: NARHAD; ISSN: 0305-1048  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To exert control over RNA folding and catalysis, both mol. engineering strategies and in vitro selection techniques have been applied toward the development of allosteric ribozymes whose activities are regulated by the binding of specific effector mols. or ligands. We now describe the isolation and characterization of a new and considerably versatile RNA element that functions as a communication module to render disparate RNA folding domains interdependent. In contrast to some existing communication modules, the novel 9-nt RNA element is demonstrated to function similarly between a variety of catalysts that include the hepatitis delta virus, hammerhead, X motif and Tetrahymena **group I** ribozymes, and various ligand-binding domains. The data support a mechanistic model of RNA folding in which the element is comprised of both canonical and non-canonical base pairs and an unpaired nucleotide in the active, effector-bound conformation. Aside from enabling effector-controlled RNA function through rational design, the element can be utilized to identify sites in large RNAs that are susceptible to effector regulation.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:22547 CAPLUS  
DOCUMENT NUMBER: 138:282224  
TITLE: **Group I** aptazymes as genetic regulatory switches  
AUTHOR(S): Thompson, Kristin M.; Syrett, Heather A.; Knudsen, Scott M.; Ellington, Andrew D.  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX, 78712, USA  
SOURCE: BMC Biotechnology [online computer file] (2002), 2, No pp. given  
PUBLISHER: BioMed Central Ltd.  
DOCUMENT TYPE: Journal; (online computer file)  
LANGUAGE: English  
AB Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated *in vitro* by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication *in vivo*. We attempted to generate **Group I** self-splicing introns that were activated by a small organic effector, theophylline, and to show that such **Group I** aptazymes could mediate theophylline-dependent splicing *in vivo*. By appending **aptamers** to the **Group I** self-splicing intron, we have generated a **Group I** aptazyme whose *in vivo* splicing is controlled by exogenously added small mols. Substantial differences in gene regulation could be observed with compds. that differed by as little as a single Me group. The effector-specificity of the **Group I** aptazyme could be rationally engineered for new effector mols. In conclusion, **group I** aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies.  
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1997:390948 CAPLUS  
DOCUMENT NUMBER: 127:118625  
TITLE: Recent solution structures of RNA and its complexes with drugs, peptides and proteins  
AUTHOR(S): Ramos, Andres; Gubser, Charles C.; Varani, Gabriele  
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Cambridge, CB2 2QH, UK  
SOURCE: Current Opinion in Structural Biology (1997), 7(3), 317-323  
PUBLISHER: COSBEP; ISSN: 0959-440X  
DOCUMENT TYPE: Current Biology  
LANGUAGE: Journal; General Review  
English  
AB A review with 59 refs. The past two years have seen remarkable progress in the study of RNA structure: the predicted era of RNA structural biol. has arrived. Crystallog. structures of the hammerhead ribozyme and of a large subunit of a **group I** self-splicing intron have begun to reveal the structural basis of RNA enzymic activity. A remarkable number of structures of small RNAs and of complexes with drugs, peptides and one protein domain have been determined by NMR.  
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1997:490324 CAPLUS  
TITLE: New insights into RNA folding from structures of small RNAs  
AUTHOR(S): Feigon, J.

CORPORATE SOURCE: Department Chemistry & Biochemistry, University California, Los Angeles, CA, 90095-1569, USA  
SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), PHYS-162. American Chemical Society: Washington, D. C.  
CODEN: 64RNAO

DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English

AB Recent solution NMR structures of RNA oligonucleotides provide a wealth of information in the factors underlying RNA folding and stability. We have used multinuclear, multidimensional NMR to solve the structure of several RNAs, including an ATP-binding RNA **aptamer**, a rRNA stem-loop, and the tetraloop receptor of a **Group I** intron. The structures, and what they tell us about RNA folding, will be discussed.

L8 ANSWER 10 OF 10 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2004278987 EMBASE  
TITLE: **Group I** aptazymes as genetic regulatory switches.  
AUTHOR: Thompson K.M.; Syrett H.A.; Knudsen S.M.; Ellington A.D.  
CORPORATE SOURCE: A.D. Ellington, Department of Chemistry/Biochemistry, Inst. for Cellular/Molecular Biology, University of Texas at Austin, Austin, TX 78712, United States.  
andy.ellington@mail.utexas.edu  
SOURCE: BMC Biotechnology, (4 Dec 2002) 2/- (12p).  
Refs: 43  
ISSN: 1472-6750 CODEN: BBMIE6  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Background: Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated *in vitro* by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication *in vivo*. We attempted to generate **Group I** self-splicing introns that were activated by a small organic effector, theophylline, and to show that such **Group I** aptazymes could mediate theophylline-dependent splicing *in vivo*. Results: By appending **aptamers** to the **Group I** self-splicing intron, we have generated a **Group I** aptazyme whose *in vivo* splicing is controlled by exogenously added small molecules. Substantial differences in gene regulation could be observed with compounds that differed by as little as a single methyl group. The effector-specificity of the **Group I** aptazyme could be rationally engineered for new effector molecules. Conclusion: **Group I** aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies. .COPYRGT. 2002 Thompson et al; licensee BioMed Central Ltd.

=> d his

(FILE 'HOME' ENTERED AT 10:34:39 ON 01 MAR 2005)

FILE 'MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 10:36:08 ON 01 MAR 2005

L1 2528 S GROUP I INTRON  
L2 3305 S APTAMER  
L3 152309 S EFFECTOR  
L4 1 S L1 AND L2 AND L3  
L5 10 S L1 AND L2  
L6 6 DUP REM L5 (4 DUPLICATES REMOVED)

L7 14 GROUP I AND APTAMER  
L8 10 DUP REM L7 (4 DUPLICATES REMOVED)

=> group I and theophy?  
L9 122 GROUP I AND THEOPHY?

=> del L9  
DELETE L9? (Y) /N:y

=> L1 and theophy?  
L9 3 L1 AND THEOPHY?

=> dup rem L9  
PROCESSING COMPLETED FOR L9  
L10 3 DUP REM L9 (0 DUPLICATES REMOVED)  
ANSWERS '1-3' FROM FILE CAPLUS

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L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:261999 CAPLUS  
DOCUMENT NUMBER: 138:282303  
TITLE: Regulatable ribozymes and DNAzymes and their use in regulation of cellular product levels or screening for cells producing particular bioproducts  
INVENTOR(S): Wilson, Charles; Cload, Sharon T.; Keefe, Anthony D.  
PATENT ASSIGNEE(S): Archemix Corporation, USA  
SOURCE: PCT Int. Appl., 128 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003027310	A2	20030403	WO 2002-US30458	20020924
WO 2003027310	A3	20030626		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,  
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-324715P P 20010924  
AB Compns. and methods are provided to make, isolate, characterize and use regulatable, catalytically active nucleic acids (RCANA). The present invention is directed to RCANA that transduce mol. recognition into catalysis. Also, RCANAs according to the invention can be used as regulatory elements to control the expression of one or more genes in a metabolic pathway. RCANAs can also be used as regulated selectable markers to create a selective pressure favoring (or disfavoring) production of a targeted bioprotein. In addition, the RCANAs can be used to regulate the activity of a reporter gene in cells and thereby provide a means to screen a population of cells for a cell producing a desired bioprotein. Thus, a selection scheme to provide protein-regulatable ribozymes was developed and applied to tyrosyl-tRNA synthetase-regulated **group I intron** ND1 of Neurospora to produce hen egg white lysozyme-regulated ligase. This ribozyme exhibited a 3100-fold activation by lysozyme, ligating with a rate of 0.6 h<sup>-1</sup> in the presence of lysozyme but only 0.0002 h<sup>-1</sup> in its absence.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2003:22547 CAPLUS

DOCUMENT NUMBER: 138:282224  
TITLE: Group I aptazymes as genetic regulatory switches  
AUTHOR(S): Thompson, Kristin M.; Syrett, Heather A.; Knudsen, Scott M.; Ellington, Andrew D.  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Institute for Cellular and Molecular Biology, University of Texas at Austin, Austin, TX, 78712, USA  
SOURCE: BMC Biotechnology [online computer file] (2002), 2, No pp. given  
CODEN: BBMIE6; ISSN: 1472-6750

PUBLISHER: URL: <http://www.biomedcentral.com/1472-6750/2/21>  
DOCUMENT TYPE: BioMed Central Ltd.  
LANGUAGE: English

AB Allosteric ribozymes (aptazymes) that have extraordinary activation parameters have been generated in vitro by design and selection. For example, hammerhead and ligase ribozymes that are activated by small organic effectors and protein effectors have been selected from random sequence pools appended to extant ribozymes. Many ribozymes, especially self-splicing introns, are known control gene regulation or viral replication in vivo. We attempted to generate Group I self-splicing introns that were activated by a small organic effector, **theophylline**, and to show that such Group I aptazymes could mediate **theophylline**-dependent splicing in vivo. By appending aptamers to the Group I self-splicing intron, we have generated a Group I aptazyme whose in vivo splicing is controlled by exogenously added small mols. Substantial differences in gene regulation could be observed with compds. that differed by as little as a single Me group. The effector-specificity of the Group I aptazyme could be rationally engineered for new effector mols. In conclusion, group I aptazymes may find applications as genetic regulatory switches for generating conditional knockouts at the level of mRNA or for developing economically viable gene therapies.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:924000 CAPLUS

DOCUMENT NUMBER: 136:66194

TITLE: Methods for selection and use of regulatable, catalytically active nucleic acids (RCANA) or aptazymes

INVENTOR(S): Ellington, Andrew D.; Hesselberth, Jay; Marshall, Kris; Robertson, Michael; Sooter, Letha; Davidson, Eric; Cox, J. Colin; Reidel, Timothy

PATENT ASSIGNEE(S): Board of Regents the University of Texas System, USA

SOURCE: PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096559	A2	20011220	WO 2001-US19302	20010614
WO 2001096559	A3	20030710		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2412664	AA	20011220	CA 2001-2412664	20010614
EP 1364009	A2	20031126	EP 2001-946430	20010614

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004515219 T2 20040527 JP 2002-510676 20010614

PRIORITY APPLN. INFO.: US 2000-212097P P 20000615

WO 2001-US19302 W 20010614

AB Compns. and methods are provided to make, isolate, characterize and use regulatable, catalytically active nucleic acids (RCANA). RCANA may be used for regulating gene expression and in assays to detect the presence of ligands or to detect activation by an effector of an RCANA bound to a solid support such as a chip or multi-well plate. Also disclosed are compns. and methods for automating the selection procedures of the present invention. In addition, the invention claims diagnostic and therapeutic applications. One example of the invention involves construction of an RCANA by PCR using primers from the P6 region of the Group I ribozyme, cloning of the RCANA or in vitro transcription followed by RNA purification, and demonstration of **theophylline**-dependent splicing activity towards the bacteriophage T4 gene td intron in vivo or in vitro. As another example of the invention, an RCANA was isolated with an activity that was increased 75,000-fold in the presence of its protein effector, Neurospora crassa mitochondrial tyrosyl tRNA synthetase (Cyt18). This RCANA was selected from a pool of randomized sequences spanning the catalytic core of L1 ligase by selecting for the ability to ligate an oligonucleotide tag in the presence of the Cyt18 effector and affinity capture of the oligonucleotide tag. The in vitro selection can be automated by immobilization of targets on beads and high-stringency washes to remove non-binding species. Activity of another protein-dependent ribozyme was increased 3,500-fold in the presence of hen egg white lysozyme. The lysozyme-dependent ribozyme was also activated by turkey egg white lysozyme but not by T4 lysozyme and was inhibited by a lysozyme-specific RNA binding species. A peptide-dependent RCANA was isolated with an 18,000-fold increase in its activity in the presence of the arginine-rich motif (ARM) from the HIV-1 Rev protein but not the ARM from HTLV-I Rex protein.